October 15, 1958

Dr. Frank J. Dixon
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Dear Dr. Dixon:

Thank you very much for your letter of September 23rd, and for the accompanying reprints which I have studied with great interest. I am looking forward to an opportunity to discuss these problems with Dr. Talmage at close hand when he visits us for a day next month. Meanwhile I would comment on one point raised in your own letter. I would agree that the elimination of normal globulins furnishes a rather weak model for the further stimulation of antibody and in Burnet's proposition, and my revision of it, this is replaced by a direct stimulation of potential antibody forming cells by virtue of the reaction of antigen with some form of antibody within these cells. Waksman's recent observations of what may be a proliferative response of sensitized cells, and recent hints that at early stages of antibody formation sensitivity of lymphoid cells may be a general phenomenon, may lend some support to this idea.

The origin of the diversity in antibody forming specificity is of course an even more obscure matter. In presenting a hypermutability hypothesis I would by no means discount its rival, that the antigen directly induces the antibody specificity. However for the very sort of reasons that Talmage has enumerated, an elective hypothesis seems somewhat more attractive at the present time.

Your observations on the specificity of the secondary response are of course very pertinent to the question of the variety of antibodies that may be produced by a single cell. I am making some plans with Dr. Nossal to study this question by an extension of the techniques described in the enclosed reprint. The flagellar antigen of Salmonella adelaide is described as " fg". Fortunately we have other serotypes which can act as reagents for the f and the g factors respectively and Dr. Nossal has recently worked out techniques by which it would be possible to exhaust anti-f and anti-g differentially from single droplets. In this way it should be possible to determine whether a cell from an fg-sensitized animal can be producing at the same time specific anti-f and anti-g as well as a probable cross reacting fg component.

May I inquire if you have anything new to report with regard "lymphocyte factor" which can restore the competence of newborn ani. sustain antibody formation? I had noted your abstract on this in the Federation Proceedings but have not run across anything since then.

Yours sincerely,

Joshua Lederberg
Professor of Medical Genetics

JL/jp